DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Centers for Disease Control
and Prevention (CDC)

Memorandum

Date

From The Committee to Review the Publication *Actual Causes of Death in the United States, 2000*

Subject Committee Report

To Chief of Science
Centers for Disease Control and Prevention

PURPOSE

To transmit a report outlining the assessment and findings associated with an independent review of the paper published in March 2004, *Actual Causes of Death in the United States, 2000.*

BACKGROUND

On June 23, 2004, Dr. Stephen Thacker was asked by Dr. George Mensah, Acting Director of the Centers for Disease Control and Prevention's (CDC) National Center for Chronic Disease Prevention and Health Promotion (NCCDPHP), to chair an internal review of the paper published in March 2004, *Actual Causes of Death in the United States* (Attachment A). Following a discussion with the General Accounting Office, which had been asked to conduct a similar review by Congressman Henry A. Waxman (Attachment B), Dr. Dixie E. Snider, then Acting Chief of Science, expanded the committee to include representatives with whom he had been in contact from other operating divisions within the Department of Health and Human Services (HHS). In addition to the chairman, the committee included three scientists from CDC (but not from NCCDPHP) and scientists from the National Institutes of Health (NIH) and the Agency for Healthcare Research and Quality (AHRQ) (Attachment C). The committee was staffed by Dr. George Mensah and Mr. Sean Cucchi from NCCDPHP. Dr. Robin Ikeda from the Office of Workforce and Career Development served as the rapporteur.

The committee members were provided background materials and met by telephone on August 30, 2004. The committee met in Atlanta on September 20, 2004, and was given a specific charge (Attachment D). Presentations were made to the committee by three scientists from NCCDPHP and a consultant to the National Center for Health Statistics (NCHS) who had expressed concerns about the paper (Attachment E). The committee met with three of the authors (Drs. Mokdad, Marks, and Stroup) to address their charge and questions prompted by the CDC scientists as well as those written to the Editor, Journal of the American Medical Association (JAMA) following the March publication. (A summary of these issues had been included in the background materials provided to the committee prior to the meeting.) Two members of the committee who were not able to attend the meeting were provided with a copy of the presentations from the CDC scientists and the

SPECIFIC ISSUES

A synthesis of the committee deliberations is provided below and is framed around each of the charges given to the committee.

Charge 1: Determine whether the methodology used for this analysis was appropriate and reflected the best scientific methods available at the time of publication.

Response 1: The authors set out to replicate the 1993 paper by McGinnis and Foege, *Actual causes of death in the United States* (Attachment G). The authors viewed their replication of the 1993 paper as a review paper rather than new primary analysis. The intention to replicate the influential 1993 paper was not explicit ("a method similar to that used by McGinnis and Foege") and, in fact, there were differences; the most critical was the decision to use a method published by Allison, et al. in 1999 to estimate annual deaths attributable to obesity (Allison DB, Fontaine KR, Stevens J, Van Itallie TB. Annual deaths attributable to obesity in the United States. JAMA 1999; 282:1530-1538). That decision was based on the observation by authors that the Allison method provided an estimate close to that found in the 1993 paper and could be used as a marker for the complex, multifactorial impact of overweight, diet, physical activity, hypertension, and diabetes in an effort to avoid duplicate counting. This logic was not made explicit in the article and led some scientists to conclude that the authors were using an inappropriate analysis for overweight and obesity and not appreciating the complexity of the issue. Further, there had been some criticism of the approach used by Allison in the literature although this was not directed specifically at the Allison paper. Many of the other criticisms of the Mokdad, et al. paper had been made of the 1993 McGinnis/Foege paper, the most important being the use of different methods to estimate each of the actual causes of death. However, the same scientists felt that McGinnis and Foege were more cautious in their interpretations and that the new paper should have better reflected advances in the field since 1993. All the members of the committee acknowledged that this is a very complex area of public health and that better data sources and improved analytic tools were needed. All the committee members strongly endorsed the need for further research.

Charge 2: Determine whether sensitivity analysis could be used to assess the impact of model assumptions on the findings.

Response 2: As noted by a committee member, "sensitivity analysis would have helped the authors direct critique of the paper to the impact of some the assumptions and methodological holes on the inferences… comparability across causes, both reported and actual causes of death, applying relative risks from study populations to target populations, particularly to an older population, etc." Such analyses should be done by CDC and made available to potential users.

Charge 3: Determine whether the clearance process adhered to standard CDC practice and, specifically, if the internal policy for manuscript clearance was followed.

Response 3: The manuscript was sent to all the relevant Centers/Institute/Offices for cross clearance. After some investigation, it was determined that the National Center for HIV, STD, and TB Prevention, National Center for Infectious Diseases, and National Immunization Program all cleared although there were some comments/suggestions. Initially, NCHS, the National Center for Injury Prevention and Control (NCIPC), and the National Center for Environmental Health (NCEH) did not clear and those centers were all sent a revised manuscript that was intended to address their concerns. Dr. Stroup who had initially cleared the manuscript as the Associate Director for Science, NCCDPHP, had become an author and spoke with her counterparts at NCHS and NCEH to discuss the issues. While concerns remained, it was her impression that both centers agreed to clear the paper. Nothing further was heard from either center nor from NCIPC; hence, according to CDC policy (Attachment H), the papers were cleared. Subsequent conversations the committee chair had with the individuals involved indicated that some serious concerns remained but at least two of them indicated that they did not push further because, given the prominence and reputation of the authors, they did not feel that it would make any difference. While there does not appear to be any overt or subtle pressure placed on the scientists, the fact that senior scientists had this perception and behaved this way needs to be addressed more explicitly in CDC policies and practices. If there are questions about whether a scientist at CDC is not doing something correctly, regardless of their reputation, stature or position, those scientists viewing the work should do their best to make certain the best science is being presented by CDC.

The cross-clearance policy within NCCDPHP is that other programs within the center are provided an informational copy; there is no formal cross clearance (Attachment I). That presumably took place at the February 14, 2003, center meeting with division directors but apparently the decision did not filter down to the scientists in the program until April. The scientists expressed concerns and did meet with some of the authors but they were not convinced that their perspectives were listened to or that requests for data were acknowledged. Thus, although the authors complied with the clearance policy, the concerns of the center scientists were not addressed as well as they could have been. This resulted in a lost opportunity to improve the final product published in JAMA. Even if the authors did not know about the concerns of the program scientists until April 2003, there was sufficient opportunity to revise the paper since JAMA did not accept the paper until the end of January 2004 (Attachment J).

The committee members made several recommendations regarding clearance of scientific publications, including the implementation of a standardized electronic tracking system that might facilitate the clearance process and provide permanent, accessible documentation of critical points in the process (Attachment K). If these issues have not been addressed in the new draft CDC clearance policies, your decision to not finalize those policies until this committee had met will provide an opportunity to avoid the difficulties in this clearance process should this arise in the future. These issues might warrant discussion by the committee that developed the current draft guidelines and by the Excellence in Science Committee.

Charge 4: Comment on whether a new methodology has become available since the publication of this paper that would provide better estimates of the actual causes of death.

Response 4: There have clearly been methodological advances since the publication of the 1993 paper and the authors did use at least one of these (Allison, et al.). However, there have been other advances, and the consensus of the committee is that the McGinnis/Foege approach has served a very useful purpose but must now be replaced with more sophisticated approaches, including some published since Mokdad, et al. submitted their paper. The committee also strongly underscored the fact that much research must still be done to better understand "actual causes" of death.

Charge 5: Make recommendations on what steps the authors should take regarding the published paper.

Response 5: All committee members stated that any errors in the analysis should be corrected. During the course of this review, the authors found at least one calculation error, and they intend to submit an erratum to *JAMA*. In order to make certain no other inadvertent calculation errors have been made, the committee recommends that the authors review all the calculations with an independent CDC scientist with expertise in both epidemiology and statistics before submitting the erratum. Any additional errors should also be addressed in the erratum. The authors should also share the spreadsheet models (not just the printouts) with scientists who have raised concerns to verify whether the results are replicable. One member of the committee suggested that the authors consider conducting a thorough sensitivity analysis, having it verified and cleared by an independent body such as the committee, and then a supporting document describing the results could be posted on the Web. However, this suggestion was accompanied by a concern that this might not be feasible in a reasonable time frame. The consensus of the committee was that any effort to do additional analyses for this paper would not be advisable. Instead, they strongly felt that the effort should be directed at the fundamental research concerns that have arisen in this review.

Charge 6: Make recommendations on further research that should be undertaken related to the issues addressed in the publication under review.

Response 6: The committee uniformly and strongly endorsed the symposium which is being proposed to address future research and practice related to actual causes of death, including whether the term "actual causes" should continue to be used. One committee member's comments summarizes the perspective of the entire body: *My overall perspective is that the most important outcome of the debate engendered by this paper is to stimulate much more focused attention to improving the methodology for this field. CDC's plans to hold a workshop in this arena is a good idea. Given the research efforts at NIH, AHRQ and other DHHS agencies in this field, it would be good if this workshop could be developed as a cross agency effort. Planning the workshop as a cross agency effort may require more time and potentially delay the workshop. However, it would facilitate the discussion involving broader group of experts, generally a benefit in such a complex field.*

Specific research recommendations are summarized in Attachment L.

CONCLUSION

The paper published by Mokdad, et al., *Actual causes of death in the United States 2000,* has provoked significant controversy both inside and outside the agency. While there was at least one error in the calculations and both the presentation of the paper and limitations of the approach could have been expressed more clearly, the fundamental scientific problem centers around the limitations in both the data and the methodology in this area. Moreover, the inherent bias in the use of any measure of mortality for policy without considerations of morbidity, disability, cost, etc., must be underscored. The best use of the paper, the controversy surrounding it, and the deliberations of this committee would be to take the lead in the rapid implementation of a research program that engages all the principal investigators in this field from government, academia, and the private sector. Within CDC, the committee recommends addressing the clearance issues that have arisen from this paper to ensure that CDC policies will reflect what is best for the agency and individual scientists, including those at the highest management levels in the agency. Integrity is a core value at CDC, and as a scientific agency the integrity of our science must be protected.

Finally, all the participants in this process have been open and forthright and have been a credit to CDC, NIH, AHRQ, and HHS.

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